409. *The Nitration of 4-Aminoquinoline.*

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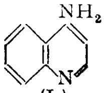
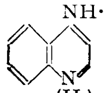
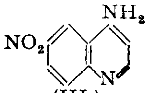
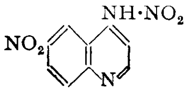
The nitration of 4-aminoquinoline is stated (Tschitschibabin *et al.*, *Ber.*, 1925, **58**, 803) to yield (III) by isomerisation of the nitroamine (II). Re-examination of the reaction has now shown that (III) undergoes further nitration to (IV); the dinitroaminoquinoline (V) formed by isomerisation of (IV) is probably 3 : 6-*dinitro*-4-*aminoquinoline.*

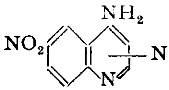
The nitration of 4-aminoquinoline, first studied by Claus and Frobenius (*J. pr. Chem.*, 1897, **56**, 202), was later examined by Tschitschibabin, Witkowsky, and Lapschin (*Ber.*, 1925, **58**, 803), who stated that the course of the reaction is represented by the stages (I) ⟶ (II) ⟶ (III).


(I.)


(II.)


(III.)


(IV.)


(V.)

As the reaction seemed to offer a ready means of preparing (III), we repeated the work of Tschitschibabin *et al.* (*loc. cit.*), but were unable to isolate (III) by any simple procedure. Furthermore, although the Russian authors claimed to have established the orientation of (III), for which they record m. p. 272°, by oxidation to 5-nitroanthranilic acid, we found (this vol., p. 1707) that 6-nitro-4-aminoquinoline, prepared from 4-chloro-6-nitroquinoline, has m. p. 312°.

We have therefore examined the reaction in some detail. A complex mixture seems to be formed, and, although a complete separation of the products was not possible, we were able to isolate (III) after prolonged fractionation, and have also established that the sequence (III) ⟶ (IV) ⟶ (V) occurs during the reaction. This conclusion was reached in the following way.

The crude nitration product, free from any unisomerised nitroamine (II or IV), could not be resolved by crystallisation, and was therefore acetylated. It was thus separated into a crystalline amphoteric product, m. p. 282—283°, which gave analytical figures in agreement with the formula $C_9H_6O_4N_4$, and a non-crystalline mixture of acetamido-compounds. The molecular formula of the substance, m. p. 282—283°, is that of a dinitroaminoquinoline, and confirmation of this was obtained by nitrating 6-nitro-4-aminoquinoline. When the reaction was carried out under conditions similar to those used for 4-aminoquinoline, the acidic 6-*nitro*-4-*nitroaminoquinoline* (IV) was isolated in high yield, and this compound was readily isomerised in acid solution to a 6 : *x*-dinitro-4-aminoquinoline (V), identical with the compound, m. p. 282—283°. We have not obtained formal proof of the orientation of this amine, but the contrast between its properties (amphoteric character, resistance to acetylation) and those shown by other nitroaminoquinolines, and the fact that 4 : 6-diamino- and 4-amino-6-acetamido-quinaldine are nitrated in the 3-position (G.P. 613,065), suggest that it is 3 : 6-*dinitro*-4-*aminoquinoline.*

When (V) was treated with 5N-hydrochloric acid under reflux, it was partly hydrolysed to an acidic compound, m. p. 354° (decomp.), of formula $C_9H_5O_5N_3$, which—if its precursor has been correctly designated—is therefore 3 : 6-*dinitro*-4-*hydroxyquinoline.* This compound was also produced, together with a mixture of bases, by acid hydrolysis of the non-crystalline acetamido-compounds (see above). The mixed bases could not be separated by crystallisation, but fractional extraction with dilute acetic acid, followed by conversion into the hydrochlorides, yielded 6-nitro-4-aminoquinoline (III), identical with the compound prepared from 4-chloro-6-nitroquinoline (Simpson and Wright, *loc. cit.*).

Experimental.

(Melting points are uncorrected.)

Nitration of 4-*Aminoquinoline.*—Nitric acid (5·6 c.c., *d* 1·40) was added during 35 minutes to a stirred solution of 4-aminoquinoline (10 g.) in concentrated sulphuric acid (55 c.c.) at −7° to + 2°. The clear solution was kept at 8° until no acid-insoluble material was obtained on dilution of a sample (1 hour); it was then poured on ice (250 g.), and the mixture basified with 20% aqueous sodium hydroxide. The solid (A) was collected, washed, and dried in a desiccator (12·1 g.); it had m. p. 250—270° (decomp.), and on repeated crystallisation gave, in poor yield, pale yellow needles, m. p. 278—281° alone and when mixed with the dinitroaminoquinoline (see below).

3(?) : 6-*Dinitro*-4-*aminoquinoline*.—The solid (A) (20 g.) was refluxed for ½ hour with acetic anhydride (60 c.c.), and the solution was left in an evacuated desiccator over sodium hydroxide for 24 hours. The solid (B) which had separated was collected (12 g.), and solvent removed from the filtrate, giving a dark brown resin (C). Continued recrystallisation of (B) from ethyl acetate and finally from aqueous acetone gave, with heavy losses, 3(?) : 6-*dinitro*-4-*aminoquinoline* as pale yellow needles, m. p. 282—283° (Found : C, 46·5; H, 2·7; N, 24·0. $C_9H_6O_4N_4$ requires C, 46·15; H, 2·6; N, 23·9%), virtually insoluble in water and in cold dilute ammonium hydroxide, but appreciably soluble in hot dilute hydrochloric acid and in hot dilute sodium hydroxide; as anticipated from its method of isolation, the compound was unaffected by boiling acetic anhydride.

3(?) : 6-*Dinitro*-4-*hydroxyquinoline*.—The resin (C) was refluxed for 35 minutes with 2N-hydrochloric acid, filtered hot (solid D), cooled, and again filtered (solid E); the filtrate was basified with ammonia, and the solid (F) collected. The solid (D) (0·9 g.) was practically insoluble in the common solvents, and was best purified by repeated dissolution in very dilute ammonium hydroxide and reprecipitation with acetic acid; in this way 3(?) : 6-*dinitro*-4-*hydroxyquinoline* was obtained as colourless needles, m. p. 352—354° (decomp.) (Found : C, 46·1; H, 2·2; N, 17·55. $C_9H_5O_5N_3$ requires C, 46·0; H, 2·1; N, 17·9%), which had no basic properties. Similar treatment of (E) (1 g.) gave a product, m. p. 312—316° (decomp.), which was extracted with hot acetic acid; the insoluble portion, after treatment with dilute ammonia and precipitation with acetic acid, had m. p. 347° (decomp.) alone and mixed with 3(?) : 6-dinitro-4-hydroxyquinoline. The same compound, m. p. and mixed m. p. 348—350° (decomp.), was obtained (30—40%) by refluxing 3(?) : 6-dinitro-4-aminoquinoline for 3 hours with 5N-hydrochloric acid (100 parts); the reaction was very slow, and at least 50% of unchanged amine (from which more hydroxy-compound was obtainable by renewed hydrolysis) was recoverable from the filtrate.

6-*Nitro*-4-*aminoquinoline*.—The solid (F) (6 g.) was extracted with 15-c.c. portions of cold 1% aqueous acetic acid until no further material was removed (13 extractions; total solids extracted = 4 g.). The material obtained by basifying the first 9 extracts was recrystallised several times from hot 2N-hydrochloric acid and then basified, yielding 6-nitro-4-aminoquinoline as an orange solid, m. p. 303—306° (decomp.), not depressed by admixture with a sample [m. p. 311—312° (decomp.)] prepared from 4-chloro-6-nitroquinoline (Simpson and Wright, *loc. cit.*); the corresponding acetyl derivative had m. p. 228—229° alone and mixed with authentic material (m. p. 228—229°; *loc. cit.*).

6-*Nitro*-4-*nitroaminoquinoline*.—Concentrated nitric acid (0·4 c.c., *d* 1·40) was added during 2 minutes to a stirred solution of 6-nitro-4-aminoquinoline (0·5 g.) in concentrated sulphuric acid (4 c.c.) at −16° to −20°. The solution was immediately poured on ice (50 g.), and the suspension made alkaline at 0° with ammonium hydroxide. The solution was filtered from a trace of insoluble material, acidified (hydrochloric acid), and the crude 6-*nitro*-4-*nitroaminoquinoline* (0·5 g.) recrystallised from aqueous acetone, from which it formed orange-yellow prismatic needles, insoluble in ether and ligroin, which decomposed at 216° without melting (Found : C, 45·6; H, 3·0; N, 23·95. $C_9H_6O_4N_4$ requires C, 46·15; H, 2·6; N, 23·9%). When it (0·2 g.) was added during 8 minutes to stirred concentrated sulphuric acid (5 c.c.) at 0—5°, a clear solution was formed, which was poured on ice (50 g.) and filtered from traces of insoluble matter. Basification and crystallisation from aqueous acetone gave yellow needles (0·13 g.) of 3(?) : 6-dinitro-4-aminoquinoline, m. p. 281—283° alone and mixed with the sample already described.

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